FIGURE 1

Human G Protein Coupled Receptor Family

(Receptors known as of January, 1999)

CLASS	LIGAND	NUMBER	TISSUE	PHYSIOLOGY	THERAPEUTICS
•Class I					
Rhodopsin like					
	•Amine				
	•Acetylcholine (muscarinic & nicotinic)	5	Brain, Nerves, Heart	Neurotransmitter	Acuity, Alzheimer's
	•Adrenoceptors				
	•Alpha Adrenoceptors	6	Brain, Kidney, Lung	Gluconeogenesis	Diabetes, Cardiovascular
	•Beta Adrenoceptors	3	Kidney, Heart	Muscle Contraction	Cardiovascular, Respiratory
	•Dopamine	5	Brain, Kidney, GI	Neurotransmitter	Cardiovascular, Parkinson's
	•Histamine	2	Vascular, Heart, Brain	Vascular Permeability	Anti-inflammatory, Ulcers
	•Serotonin (5-HT)	16	Most Tissues	Neurotransmitter	Depression, Insomnia, Analgesic
	• Peptide				
	•Angiotensin	2	Vascular, Liver, Kidney	Vasoconstriction	Cardiovascular, Endocrine
	•Bradykinin	1	Liver, Blood	Vasodilation,	Anti-inflammatory, Asthma
	•C5a anaphylatoxin	1	Blood	Immune System	Anti-inflammatory
	•Fmet-leu-phe	3	Blood	Chemoattractant	Anti-inflammatory
	•Interleukin-8	1	Blood	Chemoattractant	Anti-inflammatory
	•Chemokine	6	Blood	Chemoattractant	Anti-inflammatory
	•Orexin	2	Brain	Fat Metabolism	Obesity
	•Nociceptin	1	Brain	Bronchodilator, Pain	Airway Diseases, Anesthetic
	•CCK (Gastrin)	2	Gastrointestinal	Motility, Fat Absorption	Gastrointestinal, Obesity, Parkinson's
	•Endothelin	2	Heart, Bronchus, Brain	Muscle Contraction	Cardiovascular, Respiratory
	•Melanocortin	5	Kidney, Brain	Metabolic Regulation	Anti-inflammatory, Analgesics
	•Neuropeptide Y	5	Nerves, Intestine, Blood	Neurotransmitter	Behavior, Memory, Cardiovascular
	•Neurotensin	1	Brain,	CNS	Cardiovascular, Analgesic
	•Opioid	3	Brain,	CNS	Depression, Analgesic
	•Somatostatin	5	Brain, Gastrointestinal	Neurotransmitter	Oncology, Alzheimer's
	•Tachykinin (Substance P, NKA_1)	3	Brain Nerves	Neurohormone	Depression, Analgesic
	•Thrombin	3	Platelets, Blood Vessels	Coagulation	Anti-coagulant, Anti-inflammatory
	•Vasopressin-like	4	Arteries, Heart, Bladder	Water Balance	Anti-diuretic, Diabetic Complications
	•Galanin	1	Brain, Pancreas	Neurotransmitter	Analgesics, Alzheimer's
	•Hormone protein				
	•Follicle stimulating hormone	1	Ovary, Testis	Endocrine	Infertility
	•Lutropin-choriogonadotropic	1	Ovary, Testis	Endocrine	Infertility

•Thyrotropin	1	Thyroid	Endocrine	Thyroidism, Metabolism
•(Rhod)opsin				
•Opsin	5	Eye	Photoreception	Ophthalmic Diseases
•Olfactory	4(~1000)	Nose	Smell	Olfactory Diseases
•Prostanoid				
•Prostaglandin	5	Arterial, Gastrointestinal	Vasodilation, Pain	Cardiovascular, Analgesic
•Lysophosphatidic Acid	2	Vessels, Heart, Lung	Inflammation	Cancer, Anti-Inflammatory
•Sphingosine-1-phosphate	2	Most Cells	Cell proliferation	Cancer
•Leukotriene	1	White Blood Cells, Bronchus	Inflammation	Asthma, Rheumatoid Arthritis
•Prostacyclin	1	Arterial, Gastrointestinal	Platelet Regulation	Cardiovascular
•Thromboxane	1	Arterial, Bronchus	Vasoconstriction	Cardiovascular, Respiratory
•Nucleotide-like				
•Adenosine	4	Vascular, Bronchus	Multiple Effects	Cardiovascular, Respiratory
•Purinoceptors	4	Vascular, Platelets	Relaxes Muscle	Cardiovascular, Respiratory
•Cannabis	2	Brain	Sensory Perception	Analgesics, Memory
•Platelet activating factor	1	Most Peripheral Tissues	Inflammation	Anti-inflammatory, Anti-asthmatic
•Gonadotropin-releasing hormone like				
•Gonadotropin-releasing hormone	1	Reproductive Organs, Pituitary	Reproduction	Prostate Cancer, Endometriosis
•Thyrotropin-releasing hormone	1	Pituitary, Brain	Thyroid Regulation	Metabolic Regulation
•Growth hormone- inhibiting factor	1	Gastrointestinal	Neuroendocrine	Oncology, Alzheimer's
•Melatonin	1	Brain, Eye, Pituitary	Neuroendocrine	Regulation of Circadian Cycle
•Class II				
Secretin like				
•Secretin	1	Gastrointestinal, Heart	Digestion	Obesity, Gastrointestinal
•Calcitonin	1	Bone, Brain	Calcium Resorption	Osteoporosis
•Corticotropin releasing factor/urocortin	1	Adrenal, Vascular, Brain	Neuroendocrine	Stress, Mood, Obesity
•Gastric inhibitory peptide (GIP)	1	Adrenals, Fat Cells	Sugar/Fat Metabolism	Diabetes, Obesity
•Glucagon	1	Liver, Fat Cells, Heart	Gluconeogenesis	Cardiovascular
•Glucagon-like Peptide 1 (GLP-1)	1	Pancreas, Stomach, Lung	Gluconeogenesis	Cardiovascular, Diabetes, Obesity
•Growth hormone-releasing hormone	1	Brain	Neuroendocrine	Growth Regulation
•Parathyroid hormone	1	Bone, Kidney	Calcium Regulation	Osteoporosis
•PACAP	1	Brain, Pancreas, Adrenals	Metabolism	Metabolic Regulation
•Vasoactive intestinal polypeptide (VIP)	1	Gastrointestinal	Motility	Gastrointestinal
•ClassIII				
•Metabotropic Glutamate	7	Brain	Sensory Perception	Hearing, Vision
•$GABA_B$	1	Brain	Neurotransmitter	Mood Disorders
•Extracellular Calcium Sensing	1	Parathyroid, Kidney, GI Tract	Calcium Regulation	Cataracts, GI Tumors

Fig. 1, pg. 2

FIGURE 2

(a)
Wild-type DRY motif
D = may also be, preferably, E, L, P, Q, T, I, C, G, N, V, H, or A.
Y = may also be, preferably, W, F, S, I, Q, H, G, C, L, D, or A.
R = may also be, preferably, H, or C, or another amino acid, wherein GPCR is not constitutively desensitized

(b)
Modified DRY motif
2nd amino acid = any amino acid other than R or K, preferably A, D, E, N, and H.

FIGURE 3

The mutated amino acid at the second position of the DRY motif is underlined.

VASOPRESSIN V2 RECEPTOR - (Human)
accession P30518

R137H

```
  1 MLMASTTSAV PGHPSLPSLP SNSSQERPLD TRDPLLARAE LALLSIVFVA VALSNGLVLA
 61 ALARRGRRGH WAPIHVFIGH LCLADLAVAL FQVLPQLAWK ATDRFRGPDA LCRAVKYLQM
121 VGMYASSYMI LAMTLDHHRA ICRPMLAYRH GSGAHWNRPV LVAWAFSLLL SLPQLFIFAQ
181 RNVEGGSGVT DCWACFAEPW GRRTYVTWIA LMVFVAPTLG IAACQVLIFR EIHASLVPGP
241 SERPGGRRRG RRTGSPGEGA HVSAAVAKTV RMTLVIVVVY VLCWAPFFLV QLWAAWDPEA
301 PLEGAPFVLL MLLASLNSCT NPWIYASFSS SVSSELRSLL CCARGRTPPS LGPQDESCTT
361 ASSSLAKDTS S
```

(SEQ ID NO:1)

ALPHA-1B ADRENERGIC RECEPTOR (ALPHA 1B-ADRENOCEPTOR).
(Golden hamster)
ACCESSION P18841
R143E

```
  1 MNPDLDTGHN TSAPAQWGEL KDANFTGPNQ TSSNSTLPQL DVTRAISVGL VLGAFILFAI
 61 VGNILVILSV ACNRHLRTPT NYFIVNLAIA DLLLSFTVLP FSATLEVLGY WVLGRIFCDI
121 WAAVDVLCCT ASILSLCAIS IDEYIGVRYS LQYPTLVTRR KAILALLSVW VLSTVISIGP
181 LLGWKEPAPN DDKECGVTEE PFYALFSSLG SFYIPLAVIL VMYCRVYIVA KRTTKNLEAG
241 VMKEMSNSKE LTLRIHSKNF HEDTLSSTKA KGHNPRSSIA VKLFKFSREK KAAKTLGIVV
301 GMFILCWLPF FIALPLGSLF STLKPPDAVF KVVFWLGYFN SCLNPIIYPC SSKEFKRAFM
361 RILGCQCRSG RRRRRRRRLG ACAYTYRPWT RGGSLERSQS RKDSLDDSGS CMSGSQRTLP
421 SASPSPGYLG RGAQPPLELC AYPEWKSGAL LSLPEPPGRR GRLDSGPLFT FKLLGEPESP
481 GTEGDASNGG CDATTDLANG QPGFKSNMPL APGHF
```

(SEQ ID NO:2)

R143A

```
  1 MNPDLDTGHN TSAPAQWGEL KDANFTGPNQ TSSNSTLPQL DVTRAISVGL VLGAFILFAI
 61 VGNILVILSV ACNRHLRTPT NYFIVNLAIA DLLLSFTVLP FSATLEVLGY WVLGRIFCDI
121 WAAVDVLCCT ASILSLCAIS IDAYIGVRYS LQYPTLVTRR KAILALLSVW VLSTVISIGP
181 LLGWKEPAPN DDKECGVTEE PFYALFSSLG SFYIPLAVIL VMYCRVYIVA KRTTKNLEAG
241 VMKEMSNSKE LTLRIHSKNF HEDTLSSTKA KGHNPRSSIA VKLFKFSREK KAAKTLGIVV
301 GMFILCWLPF FIALPLGSLF STLKPPDAVF KVVFWLGYFN SCLNPIIYPC SSKEFKRAFM
361 RILGCQCRSG RRRRRRRRLG ACAYTYRPWT RGGSLERSQS RKDSLDDSGS CMSGSQRTLP
421 SASPSPGYLG RGAQPPLELC AYPEWKSGAL LSLPEPPGRR GRLDSGPLFT FKLLGEPESP
481 GTEGDASNGG CDATTDLANG QPGFKSNMPL APGHF
```

(SEQ ID NO:3)

R143H

1 MNPDLDTGHN TSAPAQWGEL KDANFTGPNQ TSSNSTLPQL DVTRAISVGL VLGAFILFAI
61 VGNILVILSV ACNRHLRTPT NYFIVNLAIA DLLLSFTVLP FSATLEVLGY WVLGRIFCDI
121 WAAVDVLCCT ASILSLCAIS ID**H**YIGVRYS LQYPTLVTRR KAILALLSVW VLSTVISIGP
181 LLGWKEPAPN DDKECGVTEE PFYALFSSLG SFYIPLAVIL VMYCRVYIVA KRTTKNLEAG
241 VMKEMSNSKE LTLRIHSKNF HEDTLSSTKA KGHNPRSSIA VKLFKFSREK KAAKTLGIVV
301 GMFILCWLPF FIALPLGSLF STLKPPDAVF KVVFWLGYFN SCLNPIIYPC SSKEFKRAFM
361 RILGCQCRSG RRRRRRRRLG ACAYTYRPWT RGGSLERSQS RKDSLDDSGS CMSGSQRTLP
421 SASPSPGYLG RGAQPPLELC AYPEWKSGAL LSLPEPPGRR GRLDSGPLFT FKLLGEPESP
481 GTEGDASNGG CDATTDLANG QPGFKSNMPL APGHF

(SEQ ID NO:4)

R143N

1 MNPDLDTGHN TSAPAQWGEL KDANFTGPNQ TSSNSTLPQL DVTRAISVGL VLGAFILFAI
61 VGNILVILSV ACNRHLRTPT NYFIVNLAIA DLLLSFTVLP FSATLEVLGY WVLGRIFCDI
121 WAAVDVLCCT ASILSLCAIS ID**N**YIGVRYS LQYPTLVTRR KAILALLSVW VLSTVISIGP
181 LLGWKEPAPN DDKECGVTEE PFYALFSSLG SFYIPLAVIL VMYCRVYIVA KRTTKNLEAG
241 VMKEMSNSKE LTLRIHSKNF HEDTLSSTKA KGHNPRSSIA VKLFKFSREK KAAKTLGIVV
301 GMFILCWLPF FIALPLGSLF STLKPPDAVF KVVFWLGYFN SCLNPIIYPC SSKEFKRAFM
361 RILGCQCRSG RRRRRRRRLG ACAYTYRPWT RGGSLERSQS RKDSLDDSGS CMSGSQRTLP
421 SASPSPGYLG RGAQPPLELC AYPEWKSGAL LSLPEPPGRR GRLDSGPLFT FKLLGEPESP
481 GTEGDASNGG CDATTDLANG QPGFKSNMPL APGHF

(SEQ ID NO:5)

angiotensin II receptor, type 1 (AT1A) [Rattus norvegicus].
ACCESSION NP_112247

R126H

1 MALNSSAEDG IKRIQDDCPK AGRHSYIFVM IPTLYSIIFV VGIFGNSLVV IVIYFYMKLK
61 TVASVFLLNL ALADLCFLLT CPLWAVYTAM EYRWPFGNHL CKIASASVTF NLYASVFLLT
121 CLSID**H**YLAI VHPMKSRLRR TMLVAKVTCI IIWLMAGLAS LPAVIHRNVY FIENTNITVC
181 AFHYESRNST LPIGLGLTKN ILGFLFPFLI ILTSYTLIWK ALKKAYEIQK NKPRNDDIFR
241 IIMAIVLFFF FSWVPHQIFT FLDVLIQLGV IHDCKISDIV DTAMPITICI AYFNNCLNPL
301 FYGFLGKKFK KYFLQLLKYI PPKAKSHSSL STKMSTLSYR PSDNMSSSAK KPASCFEVE

(SEQ ID NO:6)

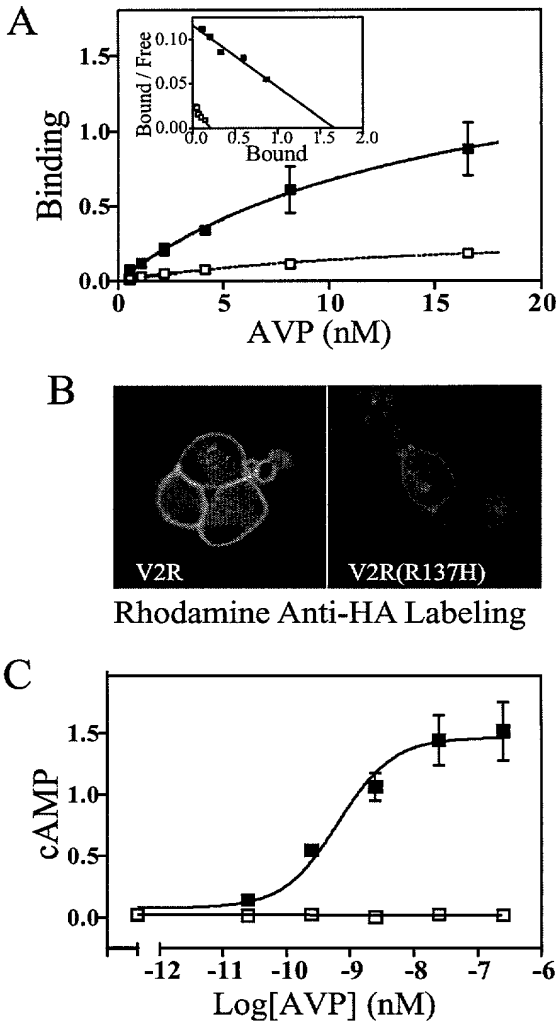
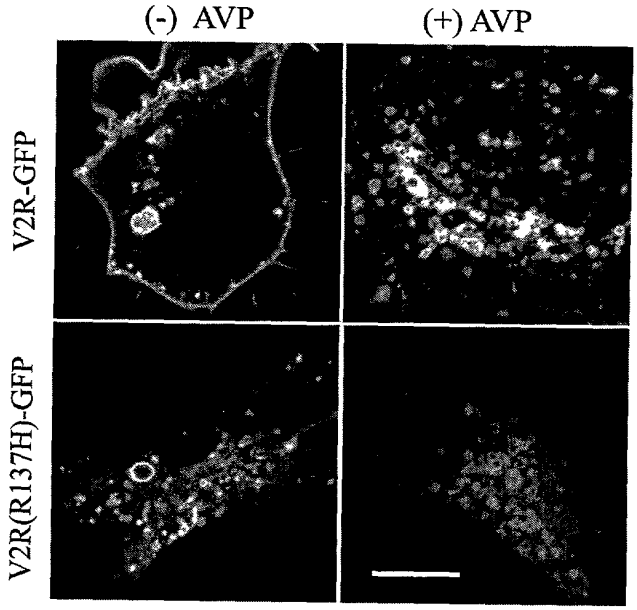
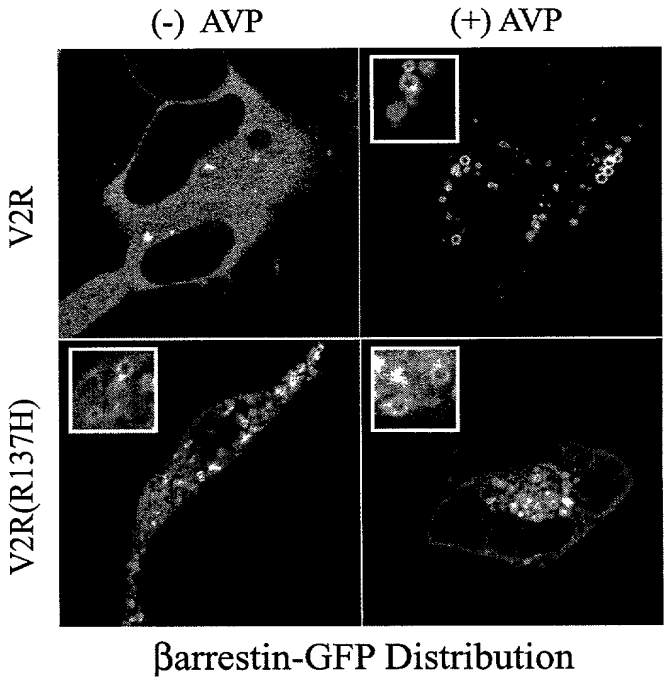

A
Binding
AVP (nM)
Bound / Free
Bound
B
V2R
V2R(R137H)
Rhodamine Anti-HA Labeling
C
cAMP
Log[AVP] (nM)

FIGURE 4



Receptor-GFP Distribution

FIGURE 5



βarrestin-GFP Distribution

FIGURE 6

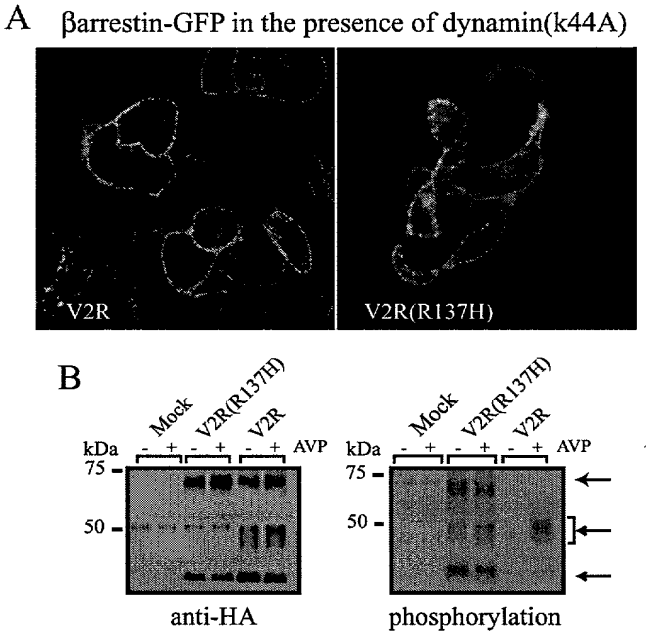

A
βarrestin-GFP in the presence of dynamin(k44A)
V2R
V2R(R137H)
B
Mock
V2R(R137H)
V2R
kDa
AVP
75
50
anti-HA
phosphorylation

FIGURE 7

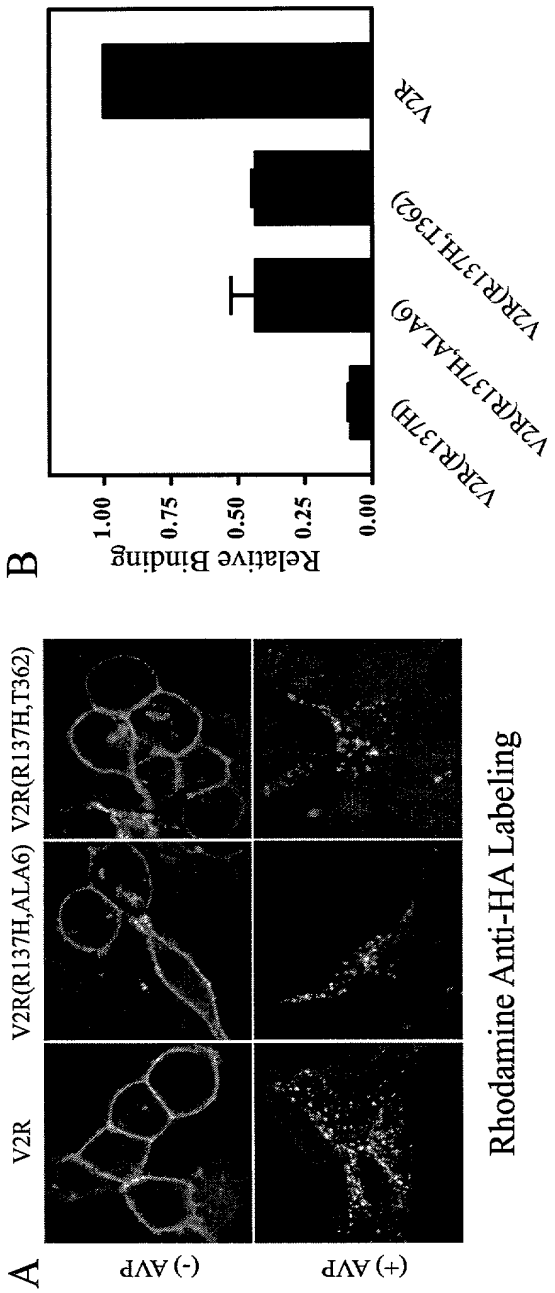

A
(-) AVP
(+) AVP
V2R
V2R(R137H,ALA6)
V2R(R137H,T362)
Rhodamine Anti-HA Labeling
B
Relative Binding
1.00
0.75
0.50
0.25
0.00
V2R
V2R(R137H,T362)
V2R(R137H,ALA6)
V2R(R137H)

FIGURE 8

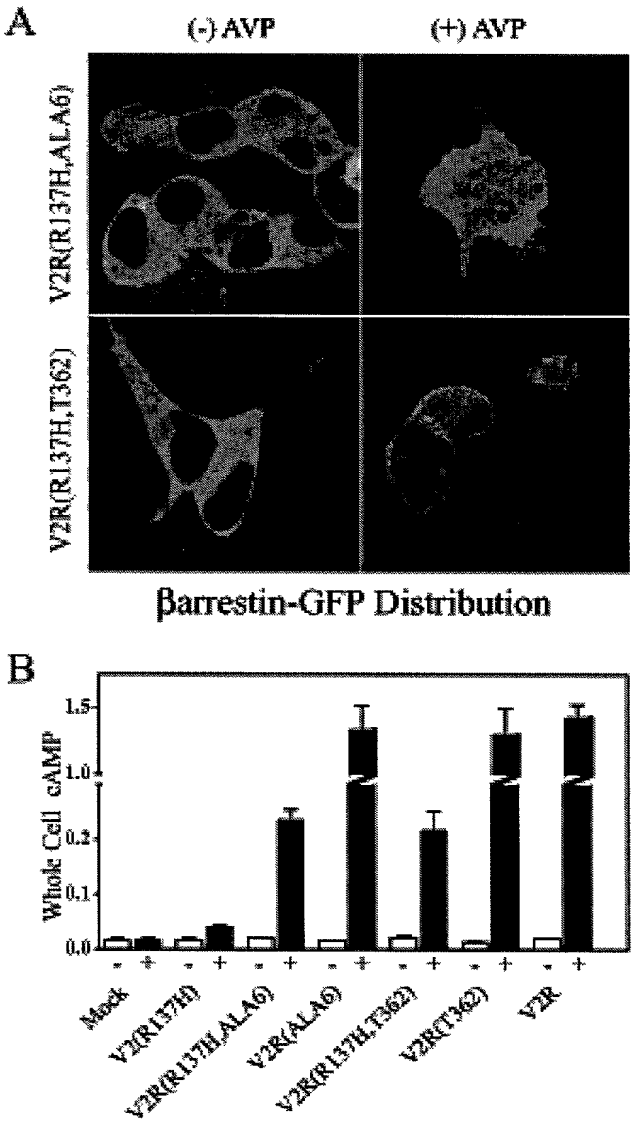

A
(-) AVP
(+) AVP
V2R(R137H,ALA6)
V2R(R137H,T362)
βarrestin-GFP Distribution
B
Whole Cell cAMP
1.5
1.0
0.2
0.1
0.0
Mock
V2R(R137H)
V2R(R137H,ALA6)
V2R(ALA6)
V2R(R137H,T362)
V2R(T362)
V2R

FIGURE 9

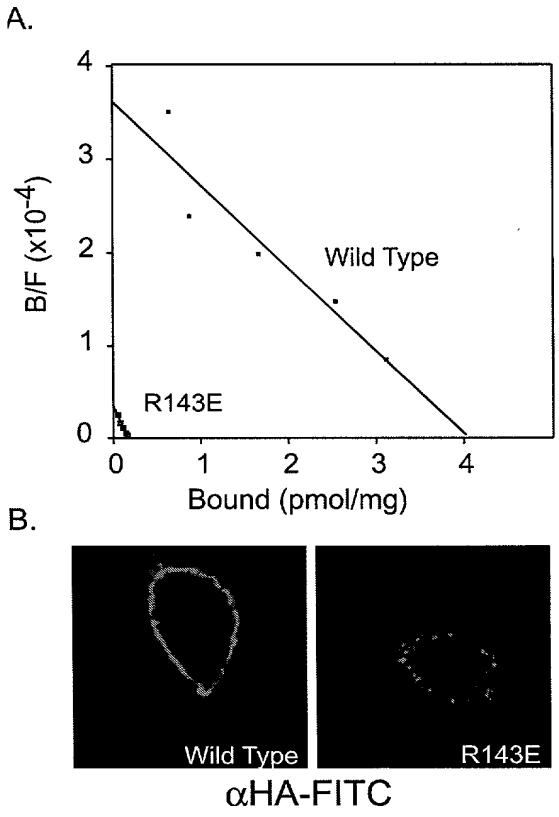

A.
B/F (x10-4)
Bound (pmol/mg)
Wild Type
R143E
0
1
2
3
4
B.
Wild Type
R143E
αHA-FITC

FIGURE 10

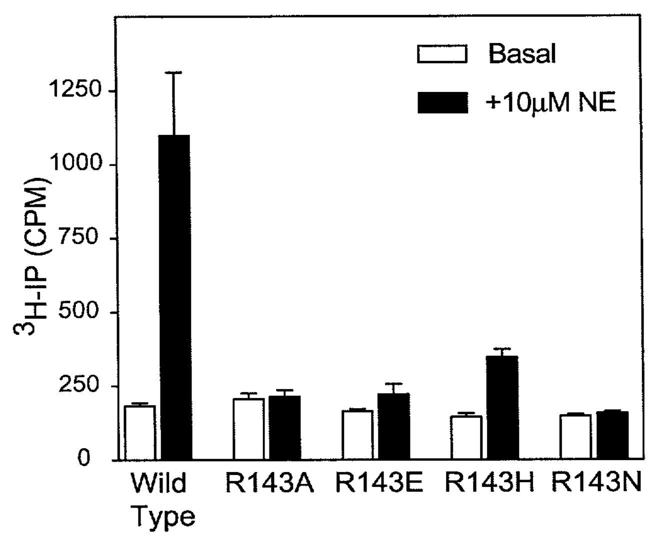
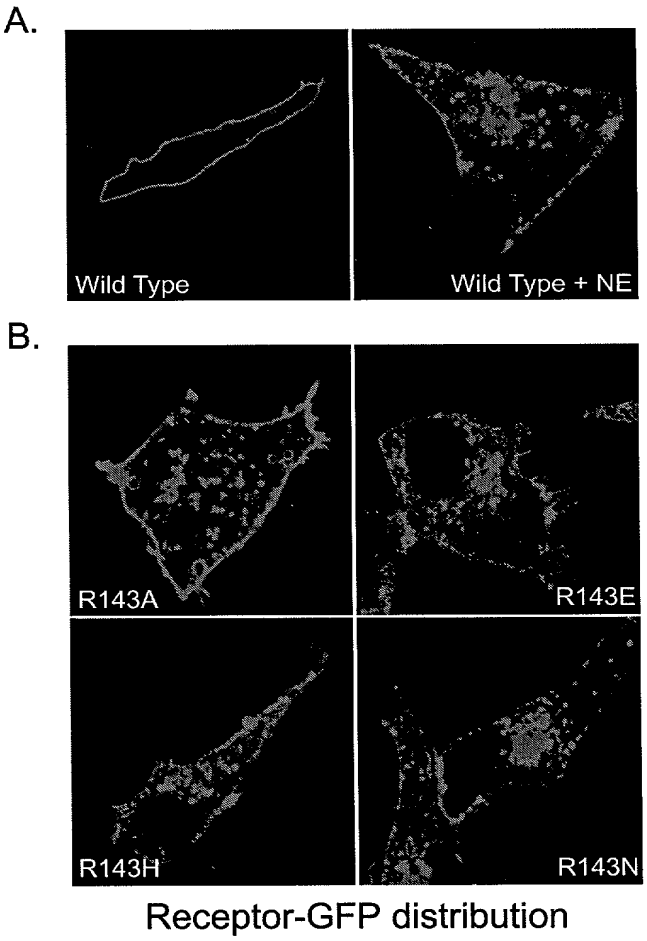


FIGURE 11



Receptor-GFP distribution

FIGURE 12

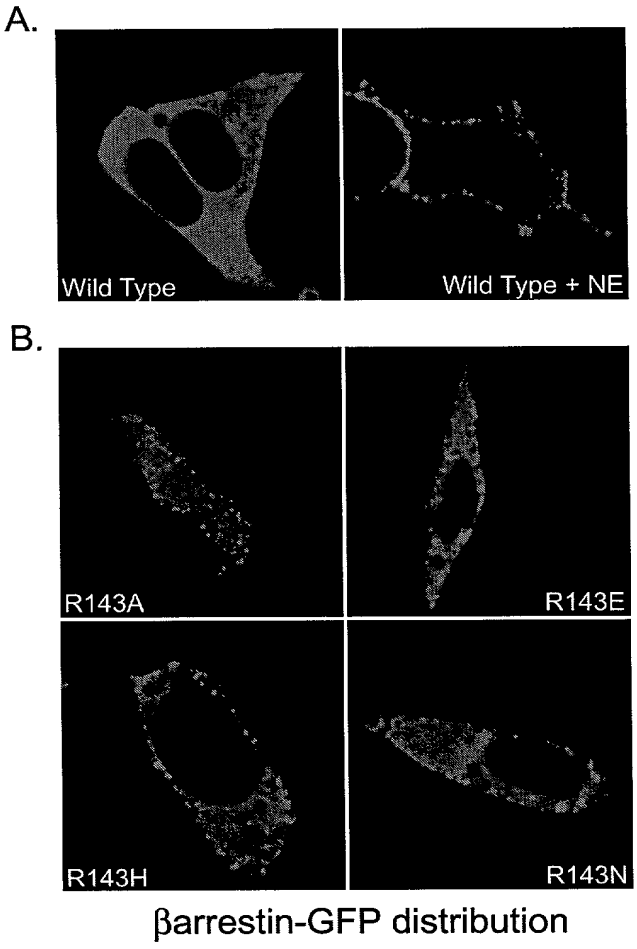

A.
Wild Type
Wild Type + NE
B.
R143A
R143E
R143H
R143N
βarrestin-GFP distribution

FIGURE 13

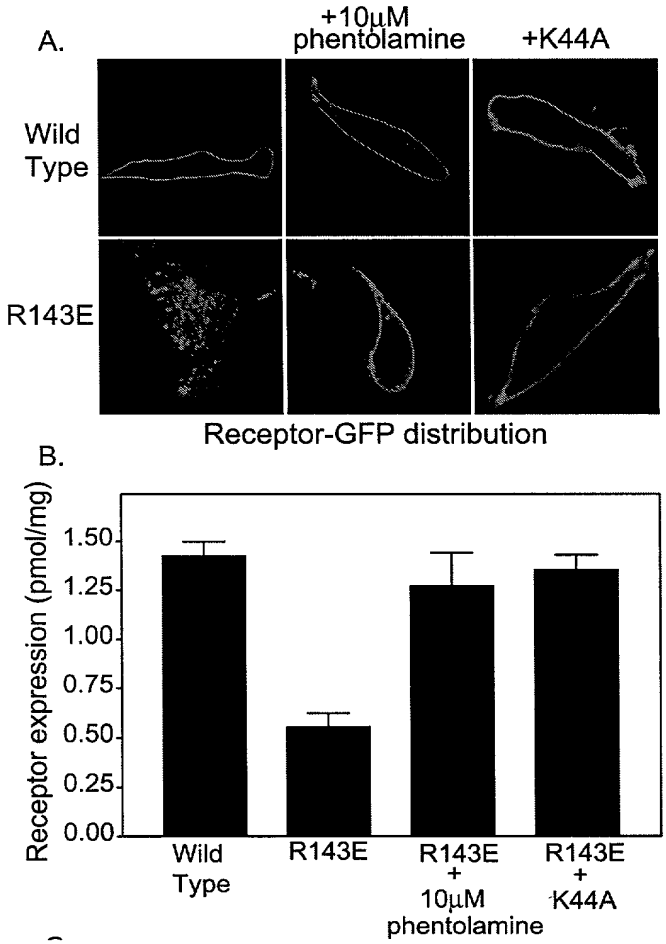

A.
+10μM phentolamine
+K44A
Wild Type
R143E
Receptor-GFP distribution
B.
Receptor expression (pmol/mg)
1.50
1.25
1.00
0.75
0.50
0.25
0.00
Wild Type
R143E
R143E + 10μM phentolamine
R143E + K44A

FIGURE 14

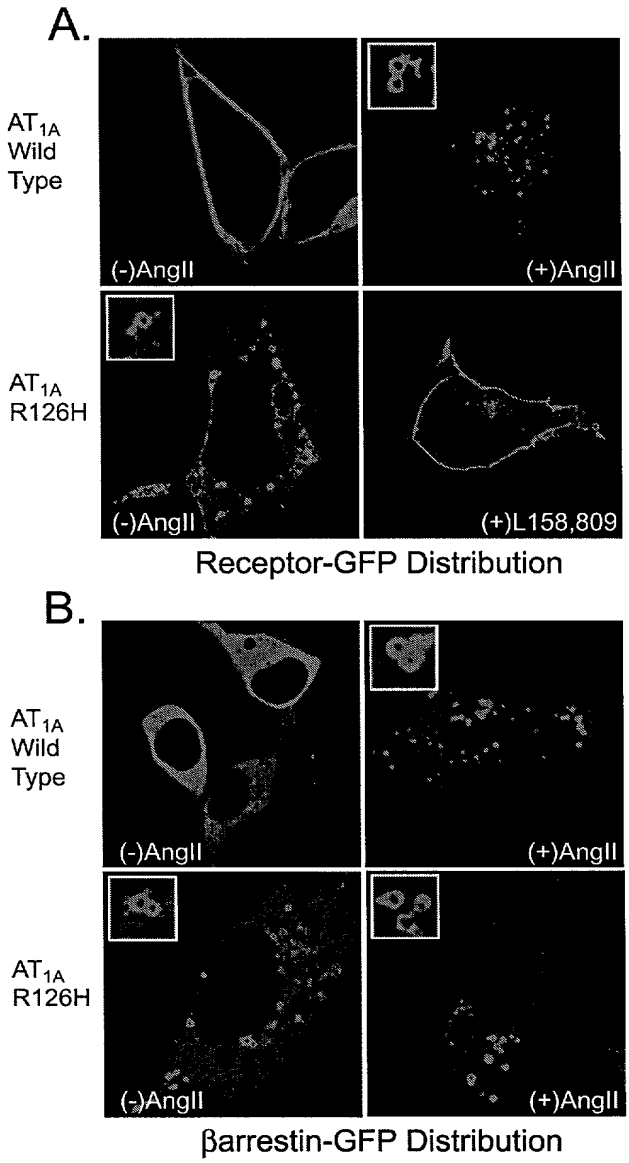

A.
AT1A Wild Type
(-)AngII
(+)AngII
AT1A R126H
(-)AngII
(+)L158,809
Receptor-GFP Distribution
B.
AT1A Wild Type
(-)AngII
(+)AngII
AT1A R126H
(-)AngII
(+)AngII
βarrestin-GFP Distribution

FIGURE 15

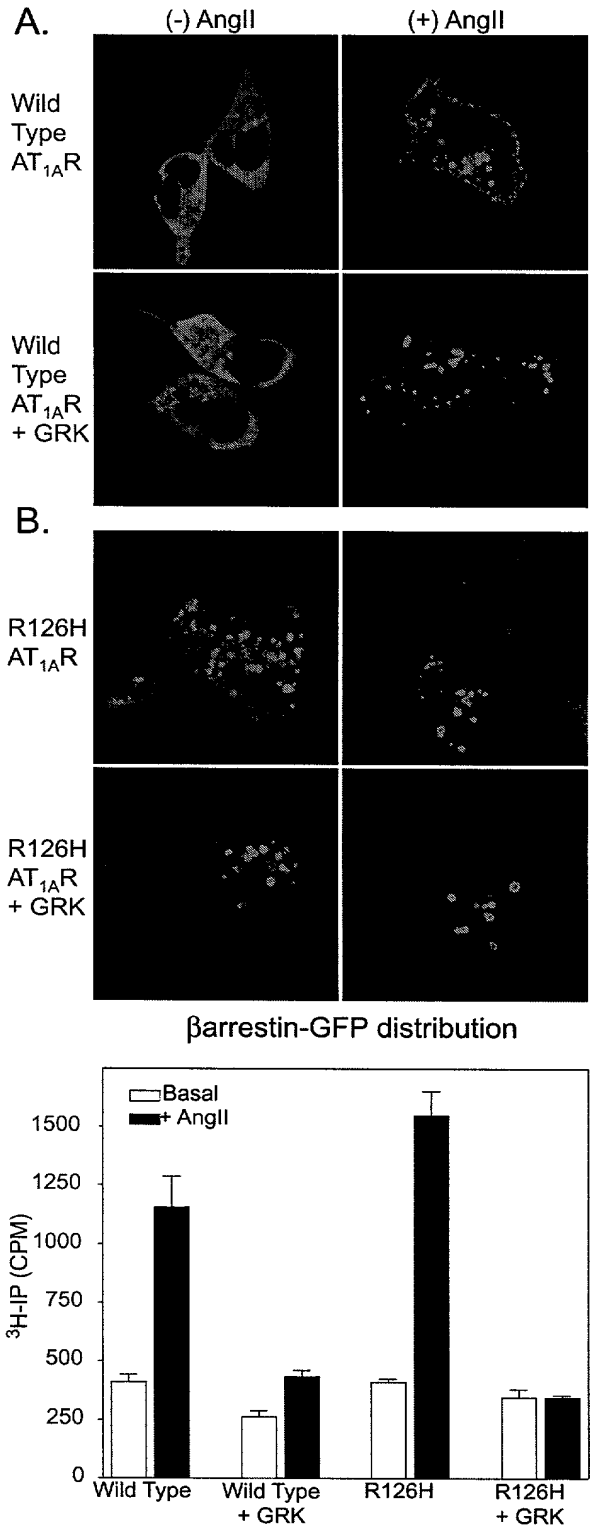

A.
(-) AngII
(+) AngII
Wild Type AT1AR
Wild Type AT1AR + GRK
B.
R126H AT1AR
R126H AT1AR + GRK
βarrestin-GFP distribution
Basal
+ AngII
3H-IP (CPM)
0
250
500
750
1000
1250
1500
Wild Type
Wild Type + GRK
R126H
R126H + GRK

FIGURE 16

FIGURE 17

Homo sapiens arginine vasopressin receptor 2
ACCESSION NM_000054

R137H

```
atgct
6 catggcgtcc accacttccg ctgtgcctgg gcatccctct ctgcccagcc
tgcccagcaa
      66 cagcagccag gagaggccac tggacacccg ggacccgctg
ctagcccggg cggagctggc
     126 gctgctctcc atagtctttg tggctgtggc cctgagcaat
ggcctggtgc tggcggccct
     186 agctcggcgg ggccggcggg gccactgggc acccatacac
gtcttcattg gccacttgtg
     246 cctggccgac ctggccgtgg ctctgttcca agtgctgccc
cagctggcct ggaaggccac
     306 cgaccgcttc cgtgggccag atgccctgtg tcgggccgtg
aagtatctgc agatggtggg
     366 catgtatgcc tcctcctaca tgatcctggc catgacgctg
gaccaccacc gtgccatctg
     426 ccgtcccatg ctggcgtacc gccatggaag tggggctcac
tggaaccggc cggtgctagt
     486 ggcttgggcc ttctcgctcc ttctcagcct gccccagctc
ttcatcttcg cccagcgcaa
     546 cgtggaaggt ggcagcgggg tcactgactg ctgggcctgc
tttgcggagc cctggggccg
     606 tcgcacctat gtcacctgga ttgccctgat ggtgttcgtg
gcacctaccc tgggtatcgc
     666 cgcctgccag gtgctcatct tccgggagat tcatgccagt
ctggtgccag ggccatcaga
     726 gaggcctggg gggcgccgca ggggacgccg gacaggcagc
cccggtgagg gagcccacgt
    786 gtcagcagct gtggccaaga ctgtgaggat gacgctagtg
attgtggtcg tctatgtgct
    846 gtgctgggca cccttcttcc tggtgcagct gtgggccgcg
tgggacccgg aggcacctct
    906 ggaaggggcg ccctttgtgc tactcatgtt gctggccagc
ctcaacagct gcaccaaccc
    966 ctggatctat gcatctttca gcagcagcgt gtcctcagag
ctgcgaagct tgctctgctg
   1026 tgcccgggga cgcaccccac ccagcctggg tccccaagat
gagtcctgca ccaccgccag
   1086 ctcctccctg gccaaggaca cttcatcgtg a
```

(SEQ ID NO:7)

Syrian golden hamster alpha-1B adrenergic receptor mRNA
ACCESSION J04084

R143H

```
        1 atgaat cccgatctgg acaccggcca caacacatca
gcacctgccc
       47 aatggggaga gttgaaagat gccaacttca ctggccccaa
ccagacctcg agcaactcca
      107 cactgcccca gctggacgtt accagggcca tctctgtggg
cctggtgctg ggcgccttca
      167 tcctctttgc cattgtgggc aacatcctgg tcatcctgtc
agtggcctgc aatcggcacc
      227 tgcggacgcc caccaactac ttcattgtca acctggccat
tgctgacctg ctgttgagtt
      287 tcacagtcct gcccttctcc gctaccctag aagtgcttgg
ctactgggtt ctggggcgca
      347 tcttctgtga catctgggca gcggtggacg tcctgtgctg
tacggcctcc atcctgagcc
      407 tatgtgccat ctccattgat cactacattg gggtgcgcta
ctctctgcag taccccactc
      467 tggtcacccg caggaaggcc atcttggcac tcctcagtgt
gtgggttttg tccacggtca
      527 tctccatcgg gcctctcctt ggatggaaag aaccagcgcc
caacgacgac aaggaatgcg
      587 gagtcaccga agaacccttc tatgccctct tttcctccct
gggctccttc tacatcccac
      647 tcgcggtcat tctggtcatg tactgccggg tctacatcgt
ggccaagagg accaccaaga
      707 acctggaggc tggagtcatg aaggagatgt ccaactccaa
ggagctgacc ctgaggatcc
      767 actccaagaa ctttcatgag gacaccctca gcagtaccaa
ggccaagggc cacaacccca
      827 ggagttccat agctgtcaaa ctttttaagt tctccaggga
aaagaaagca gccaaaacct
      887 tgggcattgt ggtcggaatg ttcatcttgt gttggctccc
cttcttcatc gctctcccac
      947 ttggctccct gttctccact ctcaagcccc cggacgccgt
gttcaaggtg gtattctggc
     1007 tgggctactt caacagctgc ctcaacccca tcatctaccc
gtgctccagc aaggagttca
     1067 agcgcgcctt catgcgtatc cttgggtgcc agtgccgtag
tggccgtcgc cgccgccgcc
     1127 gccgtcgtct gggcgcgtgc gcttacacct atcggccgtg
gacgcgcggc ggctcgctgg
     1187 agcgatcgca gtcgcggaag gactccctgg acgacagcgg
cagctgcatg agtggcagcc
     1247 agaggaccct gccctcggcg tcgcccagcc cgggctacct
gggtcgcgga gcgcagccac
     1307 cactggagct gtgcgcctac cccgaatgga aatccggggc
```

```
tctgctcagt ctgccagagc
     1367 ctccgggtcg ccgcggtcgc ctcgactctg ggcccctctt
cactttcaag ctcttgggag
     1427 agccggagag cccgggcacc gagggcgatg ccagcaatgg
gggctgcgac gcaacgaccg
     1487 acctggccaa tgggcagccc ggtttcaaga gcaacatgcc
tctggcaccc gggcactttt
     1547 ag
```

(SEQ ID NO:8)

R143A

```
        1 atgaat cccgatctgg acaccggcca caacacatca
gcacctgccc
       47 aatggggaga gttgaaagat gccaacttca ctggccccaa
ccagacctcg agcaactcca
      107 cactgcccca gctggacgtt accagggcca tctctgtggg
cctggtgctg ggcgccttca
      167 tcctctttgc cattgtgggc aacatcctgg tcatcctgtc
agtggcctgc aatcggcacc
      227 tgcggacgcc caccaactac ttcattgtca acctggccat
tgctgacctg ctgttgagtt
      287 tcacagtcct gcccttctcc gctaccctag aagtgcttgg
ctactgggtt ctggggcgca
      347 tcttctgtga catctgggca gcggtggacg tcctgtgctg
tacggcctcc atcctgagcc
      407 tatgtgccat ctccattgat gcctacattg ggtgcgcta
ctctctgcag taccccactc
      467 tggtcacccg caggaaggcc atcttggcac tcctcagtgt
gtgggttttg tccacggtca
      527 tctccatcgg gcctctcctt ggatggaaag aaccagcgcc
caacgacgac aaggaatgcg
      587 gagtcaccga agaacccttc tatgccctct tttcctccct
gggctccttc tacatcccac
      647 tcgcggtcat tctggtcatg tactgccggg tctacatcgt
ggccaagagg accaccaaga
      707 acctggaggc tggagtcatg aaggagatgt ccaactccaa
ggagctgacc ctgaggatcc
      767 actccaagaa ctttcatgag gacaccctca gcagtaccaa
ggccaagggc cacaacccca
      827 ggagttccat agctgtcaaa ctttttaagt tctccaggga
aaagaaagca gccaaaacct
      887 tgggcattgt ggtcggaatg ttcatcttgt gttggctccc
cttcttcatc gctctcccac
      947 ttggctccct gttctccact ctcaagcccc cggacgccgt
gttcaaggtg gtattctggc
     1007 tgggctactt caacagctgc ctcaacccca tcatctaccc
gtgctccagc aaggagttca
     1067 agcgcgcctt catgcgtatc cttgggtgcc agtgccgtag
```

(In line 407, the "gc" at the start of "gcctacattg" is printed bold and underlined.)

tggccgtcgc cgccgccgcc
1127 gccgtcgtct gggcgcgtgc gcttacacct atcggccgtg
gacgcgcggc ggctcgctgg
1187 agcgatcgca gtcgcggaag gactccctgg acgacagcgg
cagctgcatg agtggcagcc
1247 agaggaccct gccctcggcg tcgcccagcc cgggctacct
gggtcgcgga gcgcagccac
1307 cactggagct gtgcgcctac cccgaatgga aatccggggc
tctgctcagt ctgccagagc
1367 ctccgggtcg ccgcggtcgc ctcgactctg ggcccctctt
cactttcaag ctcttgggag
1427 agccggagag cccgggcacc gagggcgatg ccagcaatgg
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1487 acctggccaa tgggcagccc ggtttcaaga gcaacatgcc
tctggcaccc gggcactttt
1547 ag
(SEQ ID NO:9)

R143E
1 atgaat cccgatctgg acaccggcca caacacatca
gcacctgccc
47 aatggggaga gttgaaagat gccaacttca ctggccccaa
ccagacctcg agcaactcca
107 cactgcccca gctggacgtt accagggcca tctctgtggg
cctggtgctg ggcgccttca
167 tcctctttgc cattgtgggc aacatcctgg tcatcctgtc
agtggcctgc aatcggcacc
227 tgcggacgcc caccaactac ttcattgtca acctggccat
tgctgacctg ctgttgagtt
287 tcacagtcct gcccttctcc gctaccctag aagtgcttgg
ctactgggtt ctggggcgca
347 tcttctgtga catctgggca gcggtggacg tcctgtgctg
tacggcctcc atcctgagcc
407 tatgtgccat ctccattgat **gag**tacattg gggtgcgcta
ctctctgcag taccccactc
467 tggtcacccg caggaaggcc atcttggcac tcctcagtgt
gtgggttttg tccacggtca
527 tctccatcgg gcctctcctt ggatggaaag aaccagcgcc
caacgacgac aaggaatgcg
587 gagtcaccga agaacccttc tatgccctct tttcctccct
gggctccttc tacatcccac
647 tcgcggtcat tctggtcatg tactgccggg tctacatcgt
ggccaagagg accaccaaga
707 acctggaggc tggagtcatg aaggagatgt ccaactccaa
ggagctgacc ctgaggatcc
767 actccaagaa ctttcatgag gacaccctca gcagtaccaa
ggccaagggc cacaacccca

827 ggagttccat agctgtcaaa ctttttaagt tctccaggga
aaagaaagca gccaaaacct
887 tgggcattgt ggtcggaatg ttcatcttgt gttggctccc
cttcttcatc gctctcccac
947 ttggctccct gttctccact ctcaagcccc cggacgccgt
gttcaaggtg gtattctggc
1007 tgggctactt caacagctgc ctcaacccca tcatctaccc
gtgctccagc aaggagttca
1067 agcgcgcctt catgcgtatc cttgggtgcc agtgccgtag
tggccgtcgc cgccgccgcc
1127 gccgtcgtct gggcgcgtgc gcttacacct atcggccgtg
gacgcgcggc ggctcgctgg
1187 agcgatcgca gtcgcggaag gactccctgg acgacagcgg
cagctgcatg agtggcagcc
1247 agaggaccct gccctcggcg tcgcccagcc cgggctacct
gggtcgcgga gcgcagccac
1307 cactggagct gtgcgcctac cccgaatgga aatccggggc
tctgctcagt ctgccagagc
1367 ctccgggtcg ccgcggtcgc ctcgactctg ggcccctctt
cactttcaag ctcttgggag
1427 agccggagag cccgggcacc gagggcgatg ccagcaatgg
gggctgcgac gcaacgaccg
1487 acctggccaa tgggcagccc ggtttcaaga gcaacatgcc
tctggcaccc gggcactttt
1547 ag
(SEQ ID NO:10)

R143N

1 atgaat cccgatctgg acaccggcca caacacatca
gcacctgccc
47 aatggggaga gttgaaagat gccaacttca ctggccccaa
ccagacctcg agcaactcca
107 cactgcccca gctggacgtt accagggcca tctctgtggg
cctggtgctg ggcgccttca
167 tcctctttgc cattgtgggc aacatcctgg tcatcctgtc
agtggcctgc aatcggcacc
227 tgcggacgcc caccaactac ttcattgtca acctggccat
tgctgacctg ctgttgagtt
287 tcacagtcct gcccttctcc gctaccctag aagtgcttgg
ctactgggtt ctggggcgca
347 tcttctgtga catctgggca gcggtggacg tcctgtgctg
tacggcctcc atcctgagcc
407 tatgtgccat ctccattgat **aa**ctacattg gggtgcgcta
ctctctgcag taccccactc
467 tggtcacccg caggaaggcc atcttggcac tcctcagtgt
gtgggttttg tccacggtca
527 tctccatcgg gcctctcctt ggatggaaag aaccagcgcc
caacgacgac aaggaatgcg

587 gagtcaccga agaacccttc tatgccctct tttcctccct
gggctccttc tacatcccac
647 tcgcggtcat tctggtcatg tactgccggg tctacatcgt
ggccaagagg accaccaaga
707 acctggaggc tggagtcatg aaggagatgt ccaactccaa
ggagctgacc ctgaggatcc
767 actccaagaa ctttcatgag gacaccctca gcagtaccaa
ggccaagggc cacaacccca
827 ggagttccat agctgtcaaa ctttttaagt tctccaggga
aaagaaagca gccaaaacct
887 tgggcattgt ggtcggaatg ttcatcttgt gttggctccc
cttcttcatc gctctcccac
947 ttggctccct gttctccact ctcaagcccc cggacgccgt
gttcaaggtg gtattctggc
1007 tgggctactt caacagctgc ctcaacccca tcatctaccc
gtgctccagc aaggagttca
1067 agcgcgcctt catgcgtatc cttgggtgcc agtgccgtag
tggccgtcgc cgccgccgcc
1127 gccgtcgtct gggcgcgtgc gcttacacct atcggccgtg
gacgcgcggc ggctcgctgg
1187 agcgatcgca gtcgcggaag gactccctgg acgacagcgg
cagctgcatg agtggcagcc
1247 agaggaccct gccctcggcg tcgcccagcc cgggctacct
gggtcgcgga gcgcagccac
1307 cactggagct gtgcgcctac cccgaatgga aatccggggc
tctgctcagt ctgccagagc
1367 ctccgggtcg ccgcggtcgc ctcgactctg ggcccctctt
cactttcaag ctcttgggag
1427 agccggagag cccgggcacc gagggcgatg ccagcaatgg
gggctgcgac gcaacgaccg
1487 acctggccaa tgggcagccc ggtttcaaga gcaacatgcc
tctggcaccc gggcactttt
1547 ag

(SEQ ID NO:11)

Rattus norvegicus Angiotensin II receptor, type 1 (AT1AR)
ACCESSION NM_030985

R126H

1 a tggcccttaa ctcttctgct gaagatggta tcaaaagaat
42 ccaagatgac tgccccaagg ctggcaggca cagttacata
tttgtcatga tccctaccct
102 ctacagcatc atctttgtgg tgggaatatt tggaaacagc
ttggtggtga ttgtcattta
162 cttttacatg aagctgaaga ctgtggccag cgtctttctt
ctcaatctcg ccttggctga
222 cttatgcttt ttgctgactt gtcccctgtg ggcagtctat
accgctatgg agtaccgctg

282 gcccttcggc aatcacctat gtaagatcgc ttcggccagc gtgacgttca acctctacgc
342 cagtgtgttc cttctcacgt gtctcagcat cgaccactac ctggccatcg tccacccaat
402 gaagtctcgc cttcgccgca cgatgctggt ggccaaagtc acctgcatca tcatctggct
462 gatggctggc ttggccagtt tgccagctgt catccaccga aatgtatact tcatcgagaa
522 caccaatatc acagtgtgcg cgtttcatta tgagtctcgg aattcgacgc tccccatagg
582 gctgggcctt accaagaata ttctgggctt cttgttccct ttccttatca ttctcaccag
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702 aaacgatgac atctttagga taattatggc gattgtgctt ttcttcttct tttcctgggt
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822 taaaatttct gacatcgtgg acactgccat gcccatcacc atctgcatag cgtattttaa
882 caactgcctg aaccctctgt tctacggctt tctggggaag aaatttaaaa agtatttcct
942 ccagctcctg aaatatattc ccccaaaggc caagtcccac tcaagcctgt ctacgaaaat
1002 gagcacgctt tcttaccggc cttcggataa catgagctca tcggccaaaa agcctgcgtc
1062 ttgttttgag gtggagtga
(SEQ ID NO:12)